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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MATHEWS, SHEPHERD, MCKAY, & BRUNEAU, P.A.
100 THANET CIRCLE, SUITE 306
PRINCETON, NJ 08540

EXAMINER	
LI, QIAN JANICE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 06/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/845,938	KABANOV ET AL.	
	Examiner	Art Unit	
	Q. Janice Li, M.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-40,70-73 and 75-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-40,70-73 and 75-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/24/05 has been entered.

The amendment filed 3/24/05 has been entered. Claim 74 has been canceled. Claims 29, 32, 34, 37, 40, 70, 72, 77 have been amended. Claims 29-40, 70-73, 75-77 are pending and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in 3/24/05 response would be addressed to the extent that they apply to current rejection.

Claim Objections

Claim 29 is objected to because of "a molecules".

Claims 29, 32, 34 are objected to because of the "more than one plasmid or gene is expressed". A plasmid can encode a gene sequence, and express such in a cell; the plasmid itself cannot be expressed.

Claims 29 and 32 are objected to because a phase such as "wherein the composition comprises" or equivalence should be inserted in place of the second "comprising" in line 2.

Claim 77 is objected to because the claim is either incomplete or fails to further limit a previous claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30 recites the limitation "the adjuvant". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(f) he did not himself invent the subject matter sought to be patented.

Claims 29-40, 70-73, 75-77 stand rejected under 35 U.S.C. 102(e) as being anticipated by *Manthorpe et al* (US 2002/0,019,358), for reasons of record and following.

Applicants argue that *Manthorpe et al* do not teach instant claims as amended that recite more than one plasmid or gene is expressed.

In response, *Manthorpe et al* do teach "TWO OR MORE POLYNUCLEOTIDES OF THE PRESENT INVENTION CAN BE PRESENT IN A SINGLE NUCLEIC ACID CONSTRUCT, E.G., ON A SINGLE PLASMID, OR IN SEPARATE NUCLEIC ACID CONSTRUCTS, I.E. ON SEPARATE PLASMID. FURTHERMORE, ANY POLYNUCLEOTIDE MAY ENACODE A SINGLE POLYPEPTIDE, E.G., A SINGLE ANTIGEN, CYTOKINE, OR REGULATORY POLYPEPTIDE, OR MAY ENCODE TWO OR MORE POLYPEPTIDES" (paragraph 0120). Accordingly, the subject matter is fully taught by *Manthorpe et al*.

Applicants then cited a phrase in previous Office action, asserting that the state of the art is such that it is unknown that any polynucleotide would induce an immune response and activate dendritic cells.

In response, the statement was addressing the issue when the previous version of the claims was not limited to a polynucleotide expressing an antigen and a cytokine. Since the cited art clearly teach at least one polynucleotide expressing at least one antigen and at least one cytokine as currently claimed, the reference anticipates the instant claims.

Accordingly, the rejection stands.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 29, 31, 32, 34, 36, 37, 39, 40, 70, 72, 75-77 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Carson et al* (US 5,830,877), in view of *Kabanov et al* (5,656,611), and as evidenced by *Denis-Mize et al* (Gene Ther. 2000 Dec;7:2105-12).

Applicants argue neither *Carson et al* nor *Kabanov et al* teach instant claims as amended, which recite more than one plasmid or gene is expressed.

In response, *Carson et al* did teach the immunization schedules of administering an antigen and cytokine(s) together or separately. For example, *Carson et al.* states, "Particularly in the lymphatic organs, increases in the host's levels of circulating cytokines (administered with or shortly after antigen challenge) can boost the host's immune response to pathogenic antigens and (1) serve as an adjuvant for vaccines,

(2) decrease the immune response to self-antigens in autoimmune diseases, or (3) decrease the immune response to alloantigens (produced, for example, following tissue or organ transplantation)"(column 8, lines 42-53). And "For use as a tolerizing vaccine, a mixture of polynucleotides or separately coadministered group of polynucleotides may include a gene operatively encoding for an immunosuppressive cytokine (such as TGF.beta.) and a separate gene operatively encoding for a relevant histocompatibility protein. This approach could be adapted for use in inducing tolerance to foreign antigens (including alloantigens) as well as self-antigens" (paragraph bridging columns 16-17).

In view of the teaching *supra*, it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer the plasmid encoding an antigen and/or encoding a cytokine either together or separately for vaccination regimen as taught by *Carson et al* with a reasonable expectation of success.

Applicants then argued that the '611 patent stress and teach toward cationic entities to merely effect nucleic acid delivery, not for the nucleic acid formulations or activation of dendritic cell. Applicants went on to assert "enhanced ability of nucleic acids to cross cell membranes does not result in the enhanced activation of dendritic cells, and the Office action does not address this issue".

In response, since a nucleic acid asserts its function inside a cell, enhanced delivery would enhance the transgene effect expressed by the nucleic acid. When the nucleic acid expressing a transgene that activates the dendritic cell, enhanced nucleic acid delivery would logically enhance the activation of dendritic cells. Moreover, both the enhanced ability of nucleic acids delivery and the enhanced activation of dendritic cells are the intrinsic consequence of co-administering the nucleic acid and the block-copolymer, hence they are the two effects caused by the same action (method step). Applicants are reminded it is a general rule that merely discovering and claiming a new benefit to an old process cannot render the process again patentable. *In re Woodruff* 919 F. 2d 1575, 1577-78, 16 USPQ2d 1934, 1936-37 (Fed. Cir. 1990); *In re Swinehart*, 439 F. 2d 210, 213, 169 USPQ 226, 229 (CCPA 1971); and *Ex Parte Novitski*, 26 USPQ2d 1389, 1391 (Bd. Pat. App. & Int. 1993). Here, the enhanced ability of nucleic acids intercellular delivery is the motivation to combine *Carson et al* with *Kabanov et al*, even though applicants discovered another effect of the process (activating dendritic cells), it does not render the process again patentable.

Applicants also argue that the invention as currently claimed achieves unexpected results in an art that lacks predictability.

In response, it is well known in the art that administering a polynucleotide encoding an antigen induces immune response via activated dendritic cells, and it is also well known in the art that liposome enhances the function of a polynucleotide vaccine. This has been taught by *Carson et al* (column 7, t), and is now further evidenced by *Denis-Mize*, who teaches dendritic cells play a key role in antigen

presentation, but is difficult to be transduced by naked polynucleotide encoding the antigen. With the aid of a biodegradable polymer, dendritic cells are much more effectively activated for antigen presentation (e.g. fig. 4). Apparently, it is well known in the art that a polymer serves as an adjuvant to enhance the vaccine effect of a polynucleotide encoding an antigen. Thus, activation of dendritic cells does not appear to be unexpected results of instant invention.

Accordingly, the rejection stands.

Claims 29, 31, 32, 34, 36, 37, 39, 40, 70, 72, 75-77 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Mathiowitz et al* (US 6,677,313), in view of *Kabanov et al* (5,656,611), for reasons of record and *supra*.

Claims 30, 33, 35, 38, 71, and 73 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Carson et al* (US 5,830,877) or *Mathiowitz et al* (US 6,677,313), and *Kabanov et al* (5,656,611) as applied to claims 29, 31, 32, 34, 36, 37, 39, 40, 70, 72, and 75-77 above, further in view of *Alakhov et al* (6,218,438) or *Kabanov et al* (6,387,406), or *Manthorpe et al* (US 2002/0,019,358).

Applicants argue that there is no motivation to combine the references.

In response, the motivation to combine references has been indicated *supra*, i.e. enhance the efficacy of the polynucleotide. As to the particular formula, given the knowledge of the skilled in the art, it is within the levels of the skilled in the art to select a formulation known in the art, and thus this limitation falls within the bound of

optimization. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

The arguments concerning *Raz et al* are moot because the reference was not relied on for this rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 29-40 and 70-73, 75-77 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2, 3, 13, 18, 21, and 23 of U.S. Patent No. 6,359,054.

Applicants request to defer resolution of this rejection until a later time and acknowledged the willingness to file a terminal disclaimer if necessary.

Until then, for reasons of record and set forth above, the rejection stands.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Ram R. Shukla** can be reached on 571-272-0735. The fax numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1632

QJL
June 7, 2005